UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,017	04/10/2001	Dennis Cvitkovitch	1889-00401	8365

23505 7590 09/03/2004

CONLEY ROSE, P.C.
P. O. BOX 3267
HOUSTON, TX 77253-3267

EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 09/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/833,017	CVITKOVITCH ET AL.7	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,24,26,42,45,46,67 and 68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23,24,26 and 42* is/are allowed.

6)☒ Claim(s) *45,46,67 and 68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Amendment

1. Applicant's amendment filed on 6/7/04 is acknowledged.

Status of Claims

2. Claims 1-22, 25, 27-41, 43-44, and 47-66 are canceled.

Claims 45, 46, 67 and 68 have been amended.

Claims 23,24, 26 and 42 are free of prior art and are allowed.

Claims 23,24, 26, 42 45, 46, 67 and 68 are under prosecution.

Prior Citation of Title 35 Sections

3. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

New Matter Rejection Moot

4. In view of cancellation of claims 38-41 and 43-44, the new matter rejection is moot.

Claim Rejection - 35 USC 112, second paragraph Moot

5. In view of cancellation of claims 49-51 and 53-55, the rejection under 35 U.S.C. 112, second paragraph is moot.

Claim Rejections - 35 USC § 102 withdrawn

6. In view of amendment to the claims and the Declaration provided by Dr Dennis Gerald Cvitkovitch with copies of computational analysis of both GbpC and CSP and published papers on GbpC and CSP, the rejection of claims 45, 46, 67 and 68 under 35 U.S.C. 102(b) as being anticipated by Russel 1985 ((U.S.Patent 4,521,513) is withdrawn.

Claim Rejections - 35 USC 112, first paragraph maintained

7. The rejection of claims 45, 46, 67 and 68 under 35 U.S.C. 112, first paragraph written description is maintained as set forth in the previous office action.

Claims now are drawn to an isolated polypeptide that is at least 60% or 90%

Identical to SEQ ID NO: 2 or 4 and has competence signal peptide activity (considering fragments/variants)

The specification discloses a recombinant polypeptide SEQ ID NO: 2 (46 amino acids) having competence signal peptide activity to S.mutans histidine kinase. The proteolytic cleavage site was predicted to arise immediately after a double lysine consensus sequence in SEQ.ID.NO: 2, which is commonly observed at the end of leader peptide produced in all CSP of gram-positive bacteria. The leader peptide in the present invention is SEQ.ID.NO: 2. The amino acid sequence of the CSP, SEQ.ID.NO: 4 was deduced to be a 21 peptide at the carboxyl terminal of the CSP polypeptide SEQ ID NO: 2. However, the role these fragments/variants in Gram-positive bacteria has not yet been identified. Further, the specification does not disclose an isolated polypeptide having at least 60% or 90% amino acid sequence identity to SEQ ID NO: 2 or 4 and has competence signal peptide activity. Therefore, fragments/ variants of SEQ ID NO: 2 or 4 do not meet the guidelines on written description. The specification fails to disclose any deletion or change in (i) a peptide sequence of SEQ.ID.NO: 2 to obtain fragments/ variants at least 60% or 90% amino acid sequence identity to SEQ ID NO: 2 or 4 and having competence signal peptide activity or having activity for inhibiting the competence signal activity of S.mutans The specification does not describe any relevant structural or functional characteristics of fragments/variants in biofilm formation. None of the above variants meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116).

Thus, the specification fails to teach (1) an isolated polypeptide having at least 60% or 90% amino acid sequence identity to SEQ ID NO: 2 or 4 and has competence signal peptide activity sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed.

8. The rejection of c laims 45, 46, 67 and 68 under 35 U.S.C. 112, first paragraph because the specification, while being enabling for an isolated polypeptide comprising the amino acid sequence SEQ.ID.NO 2 or 4 that has S.mutans competence signal peptide activity does not reasonably provide enablement for an isolated polypeptide that has at least 60% or 90% amino acid sequence identity to SEQ ID NO: 2 or 4 is maintained as set forth in the previous office action.

The claims are discussed supra

The specification fails to provide an enabling disclosure other than peptide SEQ.ID.NO: 2 or 4 itself because it fails to provide any guidance regarding how to make and use a peptide that vary by % similarity or fragments having competence signal

peptide activity. The instant claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in In re Wands, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is identification of polypeptide compound that inhibits or disrupts microbial biofilm involved in infections. The specification indicates that the product, peptide may be used as the target for potential anti-microbial activity. The specification, however, provides no working examples demonstrating (i.e., guidance) enablement for any fragment/variants having competence signal peptide activity or having activity for inhibiting the competence signal activity. Any deletion or change in a peptide of SEQ.ID.NO: 2 or 4 is highly complex and unpredictable. As taught by the prior art that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, a stop codon in S.mutans strain JH1005, near at the end of the ComC coding sequence for CSP inserted after position 130 was found to be having low frequency (see figure 3 in Li et al 2001). Thus, it is apparent that change in a peptide leads to loss of activity of that peptide. Furthermore, it is unclear whether peptide fragments/variants can be used for inhibiting the competence signal activity and thus must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case-by-case basis.

The specification fails to provide an enabling disclosure for using peptide fragments/variants because it fails to provide guidance how a peptide fragments/variants of SEQ.ID.NO: 2 or 4 is related to CSP activity. The specification provides no disclosure how peptide fragments/variants may be used as a target for a potential biofilm formation caused by S.mutans because it fails to provide guidance whether fragments/variants has the ability to inactivate or bind to S.mutans. Absent such demonstration, the invention would require undue experimentation to practice as claimed.

Applicant's arguments filed on 6/7/04 have been fully considered but they are not deemed to be persuasive.

Applicant states that the instant specification discloses the fragments/variants and applicant followed the written description guidelines as required and the skilled person would understand the limitation of the claims as written. The specification expressly describes (Para # 38 and 54) peptides that are at least 60% or at least 90% identical to the CSP peptides SEQ ID NO. 2 or 4 and the applicant reminds the examiner Example 14 of the Written Description Guidelines published at the internet address htpp://uspto.gov/web/menu/written.pdf.

Further applicant provides the Declaration by Dr Dennis Gerald Cvitkovitch in support of enablement.

As cited by the applicant, the examiner has reviewed the Example 14 of the Written Description Guidelines and the specification Para # 38 and 54 and disagrees with the applicant for the following reasons:

The specification (Para # 38 and 54) fails to disclose

(1) The peptides that are at least 60% or at least 90% identical to SEQ ID NO. 2 or 4 have not been shown to be able to confer genetic competence to *S. mutans,* as measured by an increased ability to incorporate and express foreign genetic material, when added to cells as described in the assay of genetic competence.

(2) The peptides that are at least 60% or at least 90% identical to SEQ ID NO. 2 or 4 have not been shown to be able to confer an acid tolerance response in *S. mutans* as measured by an increase in cell survival under acidic PH conditions when added to cells i.e., they are able to stimulate genetic competence and low pH tolerance (the ability to withstand acid challenges of PH 3.5 -pH 3.0 for up to 3 hours) in *S. mutans.*

Thus, the specification fails to provide an enabling disclosure for the full scope of the claimed polypeptide that is at least 60% or 90%Identical to SEQ ID NO: 2 or 4 and has competence signal peptide activity and is able to confer genetic competence to *S. mutans.*

With respect to meeting the Written Description Guidelines, the specification should disclose (1) the structure of a claimed product (2) known or disclosed correlation between structure and function. However, the present specification does not disclose the structure of the claimed product, i.e., peptides that are at least 60% or at least 90% identical to SEQ ID NO. 2 or 4 because the specification fails to teach whether peptides comprise at least 60% or 90% of the sequence of the full length of SEQ ID NO: 2 or 4 , or peptides share at least 60% or 90% of

identity with the residues in the sequence of SEQ ID NO: 2 or 4 . In addition, there is no correlation between structure and function.

With respect to Example 14: Product by Function,

Specification: The specification does not disclose or exemplify the claimed peptide has competence signal peptide activity and is to be able to confer genetic competence to *S. mutans,* as measured by an increased ability to incorporate and express foreign genetic material, when added to cells as described in the assay of genetic competence.

The specification does not contemplate that the claimed isolated polypeptide that is at least 60% or 90%Identical to SEQ ID NO: 2 or 4 and has competence signal peptide activity to *S. mutans.* Thus, a review of the full content of the specification does not indicate that the claimed peptides have competence signal peptide activity to *S. mutans.* Moreover, variants of SEQ ID NO: 2 or 4 which have 60% or 90% identity to SEQ ID NO: 2 or 4 that retain competence signal peptide activity are not conventional in the art of genetic competence to *S. mutans.*

All the above factors have been considered in view of the level of skill and the knowledge in the art and in light of and consistent with the written description and is determined that one of skill in the art would not recognize from the disclosure that applicant was in possession of the claimed invention.

Conclusion: The disclosure does not meet the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention. The specification provides no disclosure how peptide fragments/variants may be used as a target for a potential biofilm formation caused by *S.mutans* because it fails to provide guidance whether variants has

the ability to inactivate or bind to *S.mutans*. Absent such demonstration, the invention would require undue experimentation to practice as claimed.

The examiner has considered the Declaration provided by Dr Dennis Gerald Cvitkovitch with copies of computational analysis of both GbpC and CSP and published papers on GbpC and CSP and withdrawn the rejection of claims 45, 46, 67 and 68 under 35 U.S.C. 102(b) as being anticipated by Russel 1985. However, the same Declaration is not sufficient to withdraw the written or enablement rejection as the specification does not meet the requirements of 35 USC §112 first paragraph as discussed above for the claimed peptides that are at least 60% or at least 90% identical to SEQ ID NO. 2 or 4 and has competence signal peptide activity *to S. mutans.* Further, the Declaration does not provide any evidence in support of the claimed polypeptide. Therefore, the rejections are maintained.

Remarks

9. Claims 23,24, 26 and 42 are allowed.

Claims 45, 46, 67 and 68 are rejected,

Conclusion

10. **THIS ACTION IS MADE FINAL**. See MPEP ' 706.07(a). Applicant is reminded of the extension of time policy as set forth n 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action

11 Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before final amendments is (703) 872-9306. The RightFax number for submission of after final amendments is (703) 872-9307.

12. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of the biweek.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose Telephone number is (571) 272-1600.

13. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padma Baskar